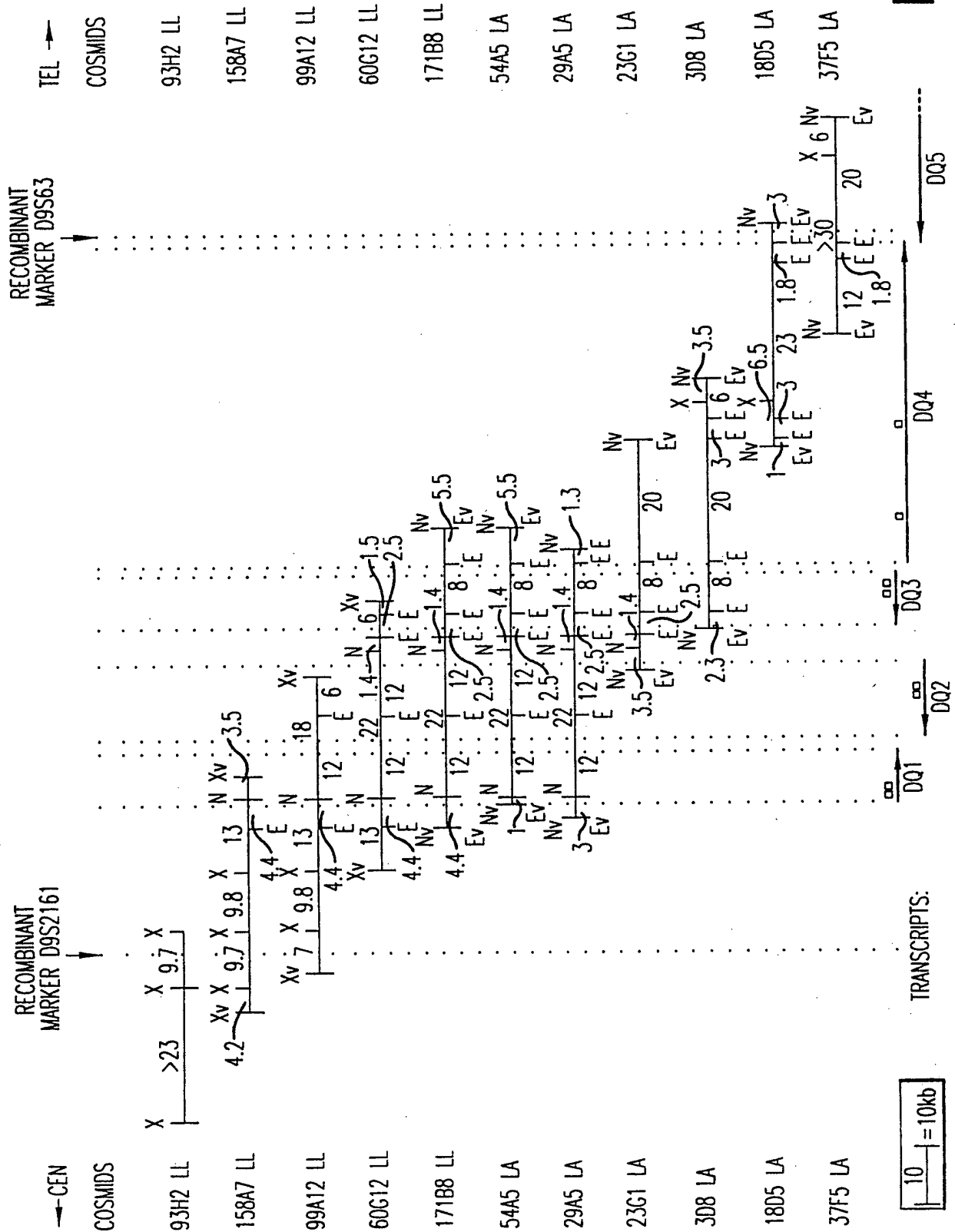
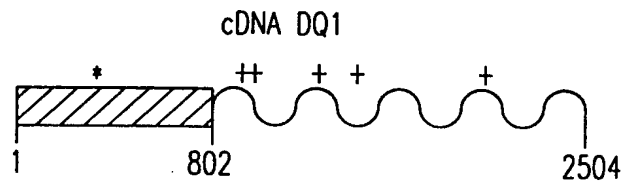


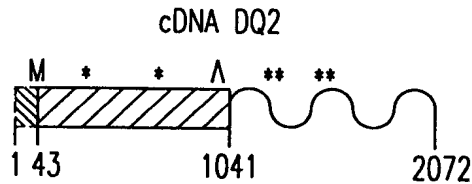
FIG. 1





Polymorphisms: C/T @ 343, proline/proline

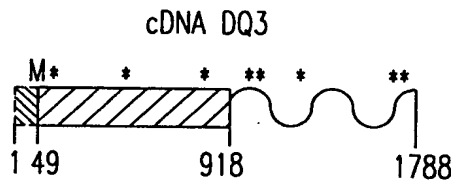
Transcript size: 2.7kb



Polymorphisms: C/T @ 288, alanine/alanine  
 G/C @ 688, aspartic acid/histidine  
 G/T @ 1232  
 C/G @ 1255  
 del/T @ 1464  
 T/A @ 1495

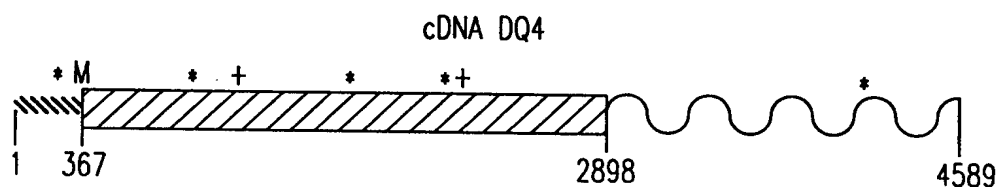
Transcript size: 2.2kb, 1.4kb

Mutation: del/GAG @ 946, del/glutamic acid



Polymorphisms: A/G @ 156, glutamic acid/glutamic acid  
 A/G @ 420, lysine/lysine  
 T/C @ 801, glycine/glycine  
 AC/CT @ 1005  
 G/A @ 1063  
 (T)<sub>n</sub> @ 1273  
 T/A @ 1724  
 A/G @ 1751

Transcript size: 1.8kb



Polymorphisms: G/A @ 225  
 C/T @ 840, alanine/alanine  
 G/A @ 1696, valine/isoleucine  
 C/T @ 2172, histidine/histidine  
 G/A @ 4225

Transcript size: 4.5kb

FIG.2

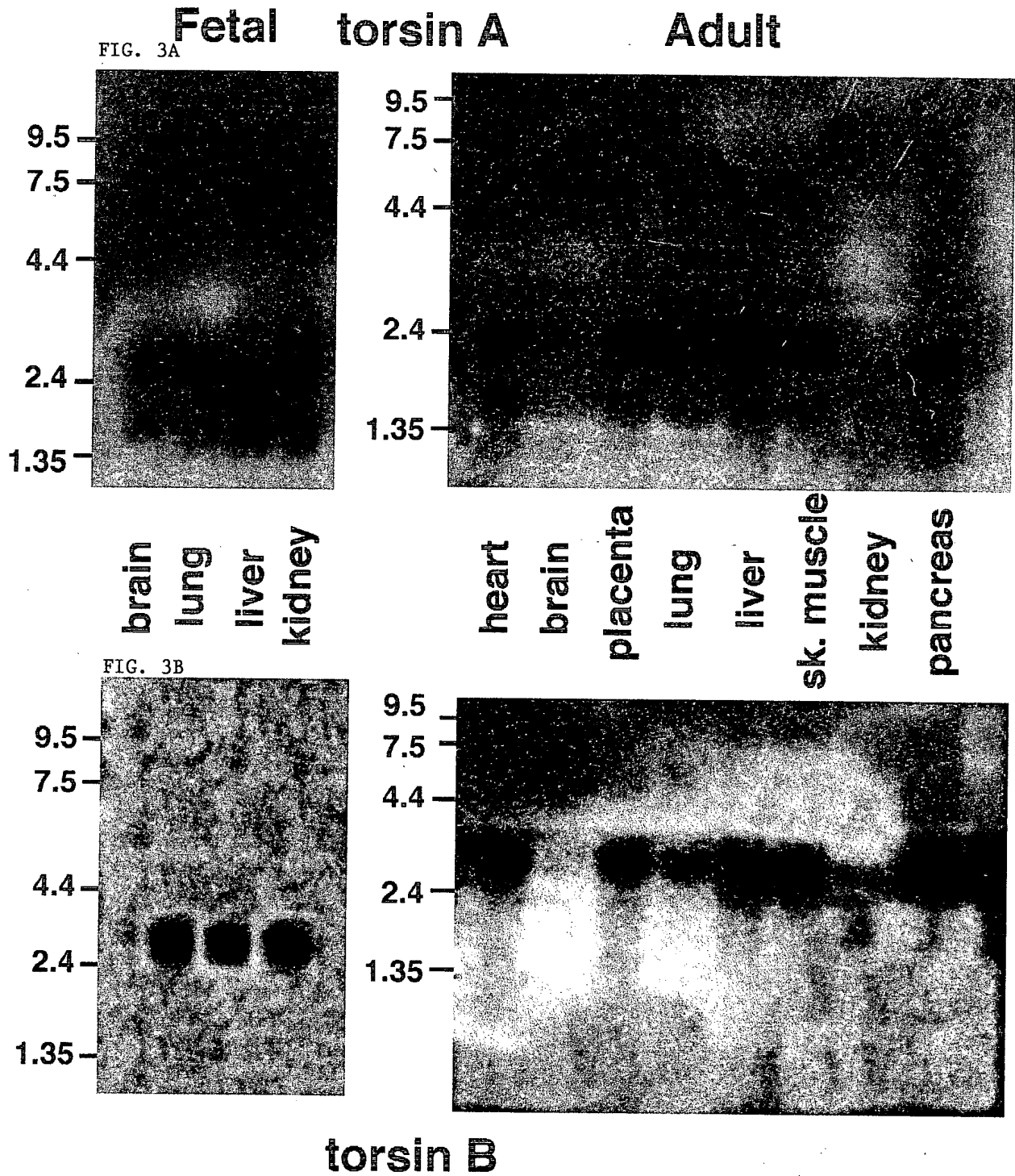
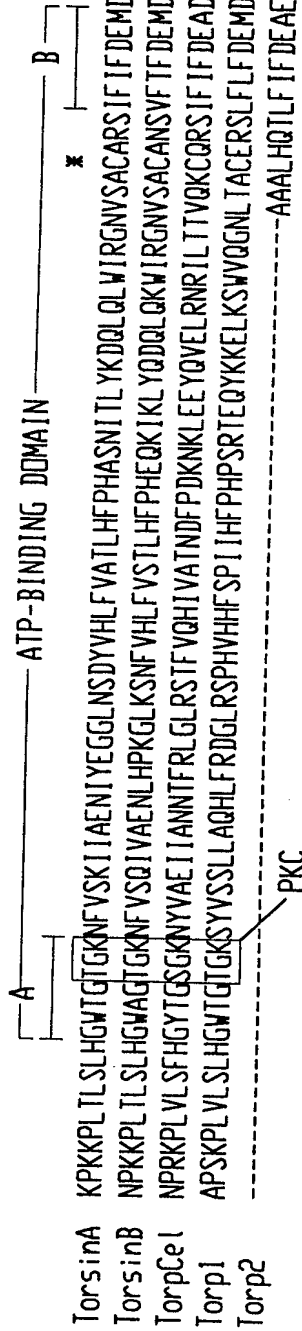


FIG. 4A

TorsinA --MKLGRAVLGLLLAPSVQAVEPISLGLALAGVLTGYIYP-----RLYCLFAECC-GQKRSLSREALQKDLDDNLFGGHLAKKILNAVGFINNIP  
 TorsinB -----LDLEKLFGGHLATEVIFKALTGRNNK  
 TorpCel1 MWMKLDY-VLLLLFHLCFVNTELISVITGKIKDSGTTIAISAGAFWGLKDRKCYLYECCEPDVNFNYHTLDADIANLLFGGHLVKDVVVNSIKSHWYNE  
 Torp1 -----LECDLAQHLAGGHLAKALVVKSLKAFVQDP  
 Torp2 -----



TorsinA KPKKPL T LSLHGWGTGKGFVSKIAENI YEGGLNSDYVHLF VATLHFPHASNITL YKQDQLQWTRGNVSACARSIF IFDEMCKMHAGLIDAIPFLD-YY  
 TorsinB NPCKPL T LSLHGWAGTGKGFVSDI VAENLHPKGLKSNFVHLFVSTLHFPHEQIKL YQDQLQKWTIRGNVSACANSVF TFDEMCKLHPGII DAIPFLD-YY  
 TorpCel1 NPRKPL VLSFHGYTGSGKNYYVAEITANNIFRLGLRSTFVQHI VATNDPDKNKLEEYQVELRNRIITTVQKCCORSIF IFDEADKLPEQLLGAIPFLD-YY  
 Torp1 APSKPL VLSLHGWGTGKGSYYSSLLAQHLFRDGLRSPHVHFSPIIHFPHPSRTEQYKKELKSWQGNLTACERSLFLFDEMCKLPPGLMEVLQPFLG-PS  
 Torp2 -----AAALHQTLF IFDEAEKLHPGLLEVLGPHLEERRA

SN

TorsinA DLVDGVSQKAMFIFLSNAGAERTDVALDFVRSKGQREDIKLDIEHALSVSVFNKNKSGFVHSSLIDPNLIDYFVPFLPEYKHKMCI RVEMQSRGY-  
 TorsinB EQVDGVSXXKAI FIFLSNAGGDLITKTALDFWRAGRKREDIQLKOLEPVL SVGVFNKNKHSGLVHSGLIDKNLIDYFIPFLPEYRHHVCMCVRAEMRARG-  
 TorpCel1 STISGVDFRRSIFILLSNKGGGEIARITKEQYESGYPREQLRLEAFERELMNF SYNEK-GGLQMSSELISNHLIDHFVPFLPLQREHVRSCVGYLRKRGRG  
 Torp1 WVVYGTNYRKAIFIFTSNAGGEQINQVALEAVRTNDRREEISLQVEPVI SRVMDNPQHGFVRSQIMEEHLLDVVVFPFLPLQRHHVRHCVLNELAQLGL-  
 Torp2 PEXXGLSLXWTIFLFLSNLRGDIINEVWLKLLKAGWSREEITMEHLEPHLQAEIVDDHQQLVHRSRLVKENLIDYFIPFLPEYRHHVRLCARDFAFLSQEL-

TorsinA --EIDEDIVSRVAEEMTFPKEERVFSIDKGGCTVFTKL DYYDD  
 TorsinB --AIDEDIVTRVAEEMTFPRDEKIVSDKGGCTVQSRLDFH  
 TorpCel1 DLVSNVDFVERVLNSLQYFPESKAFSSSGCKRV  
 Torp1 --EPARRWFRRCWTD-TYFPEVEQLFSSNGCKTVASRLTFFL  
 Torp2 --LYKEETLDEIAQMMVYVPKEQLFSSQGCKSIXQRIKLLPVMXG

FIG. 4A

T092F0'S012660

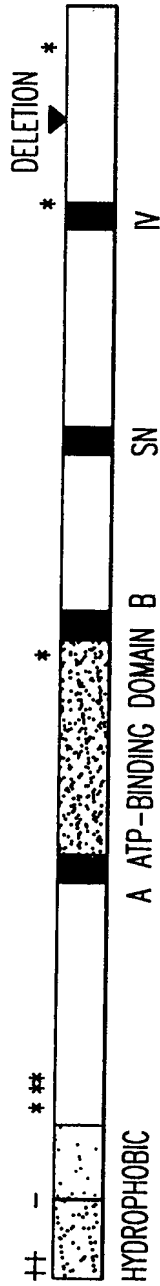


FIG. 4B

A

B

SKD3 EEHPLV-FLFLGSSGIGKTELAKQIAKYMHKDAKKGIFRLDMSEFQERHEVAKF IGSPPGYIGHEEGGQ--LTKKLKQCPNAVVL FDEVKAHPDVL TMLQLFDEGRL  
HSP-101 PQQPTGSLFLGPTGVGKTELAKALAEQLF-DNENQLVRIDMSEYMEQHSVSRL IGAPPGYVGHEEGGQ--L TEAVRRRPYSVVL FDEVEKAHTSVFNTLLQVLDGRL  
TorsinA PKKPLTSL-HGWTGTGNFVSKI I AENIYEGGLN-----SDYVHLFVATLHFPHASNITL YKQQLQWIRGNVSACARS IF IFDEMCKMHAQL IDAIKPFLD-----  
TorsinB PKKPLTSL-HGWAGTGKNFVSQI VAENLHPKGLK-----SNFVHLFVSTLHFPHQKIKL YQDQLQKWIRGNVSACANSVF IF DEMDKLHPGI IDAIKPFLD-----  
TorpC1 PRKPLVLSF-HGYTGSCKNYVAE I IANNTFRLGLR-----STFVQHIVATNDFPKNKLEEQVELRNRI LTTVQKQCRS IF IFDEADKLPEQL LGAIKPFLD-----  
Torp1 PSKPLVLSL-HGWTGTGKSYVSSLLAQHLFRDGLR-----SPHVHFSPI I HFPHPSRTEQYKKELKSWVQGNL TACERSLFLF DEMDKLPPQL MEVLQPLG-----  
Torp2 -----AAALHQTLF IFDEAEKLHPGLEVLGPHLER----

SN

IV

SKD3 TDGKGKTIDCKDAIF IMTSNVASDEIAQHALQLRQEALEM SRNRI AENLGDVQMSDKITTSKNFKENVIRPILKAHFRRDEF LGRINEI VYFLPFCHSEL IQLVNKEL  
HSP-101 TDGGQRTVDFRNTVI IMTSNLGAHELLS-GLSGKC-TMQVARDR-----VMQEVRRQ-FRPELLNRLDEI VVFDPLSHDQLRKVARLQM  
TorsinA YYDLVDGVSQKAMF IFLSNAGAERTDVALDFV-----RSKGQREDIKLDIEHALSVSVFNKK--NSGFVHSSLIDRNLI DYFVPELPLEYKHLKMCIRVEM  
TorsinB YVEQVDGVSXXKAIF IFLSNAGGDLITKTALDFV-----RAGRKREDIQLKDLEPVL SVGVFNKK--HSGLWHSGLIDKNLI DYFIPFLPLEYRHHVRCVRAEM  
TorpC1 YYSTISGVDFRRSIF ILLSNKGGGEIARTKEQY-----ESGYPREQLRLEAFERELMNF SYNEK---GGLQMSLISNHL IDHFVPELPLQREHVRSCVAYL  
Torp1 PSWVYGTNYRKAIF IFISNAGGEQINQVALEAV-----RTNRDREEISLQVEVPV I SRVMDNP--QHGFVRSGMTMEHLLDAVVPFLPLQRHHVRHCVLNEL  
Torp2 RAPEXXGLSLXWTIFLFLSNLRGDI INEVLKLL-----KAGWSREEITMEHLEPHLQAEI VDDH--RQWLWHSRLVKENLI DYFIPFLPLEYRHHVRLCARDAF

FIG. 4C

FIG. 5B

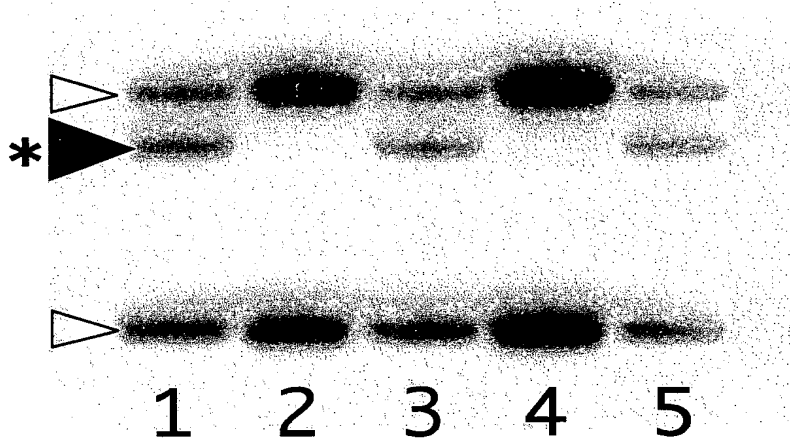


FIG. 5C

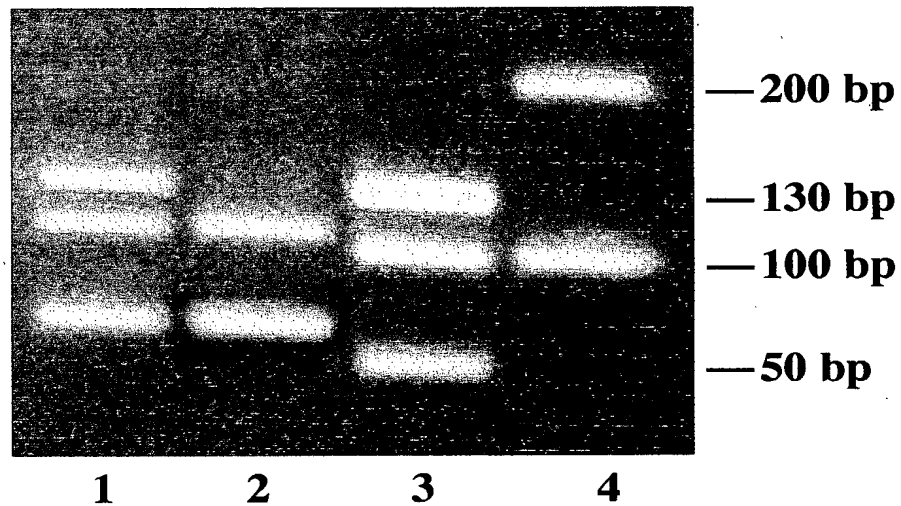
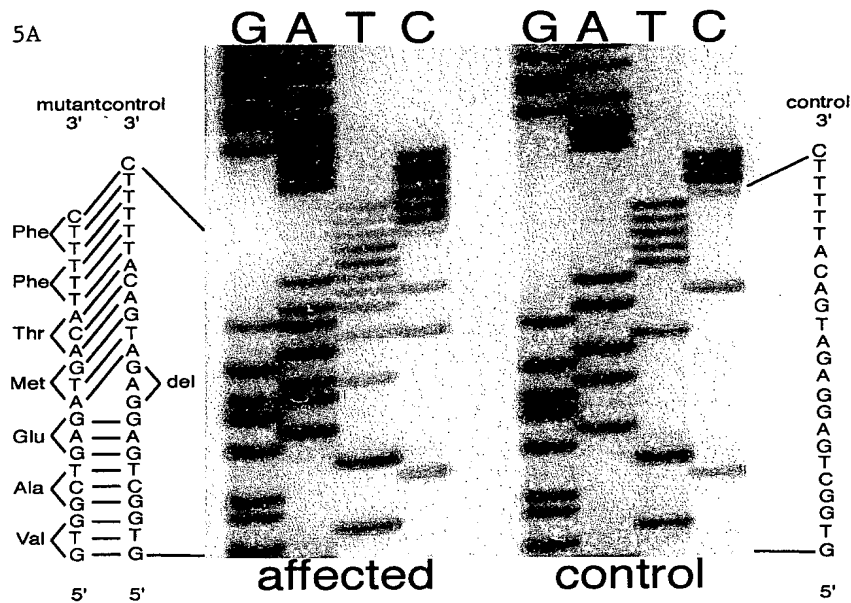


FIG. 5A



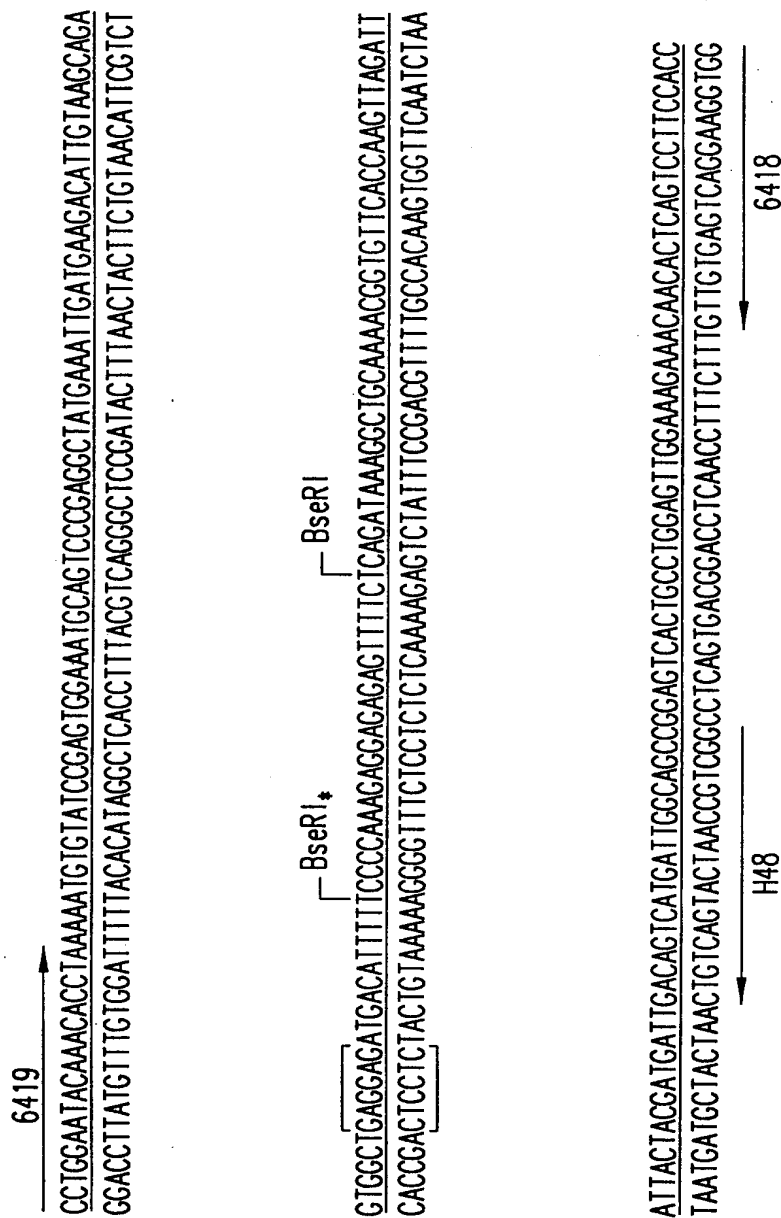


FIG. 5D





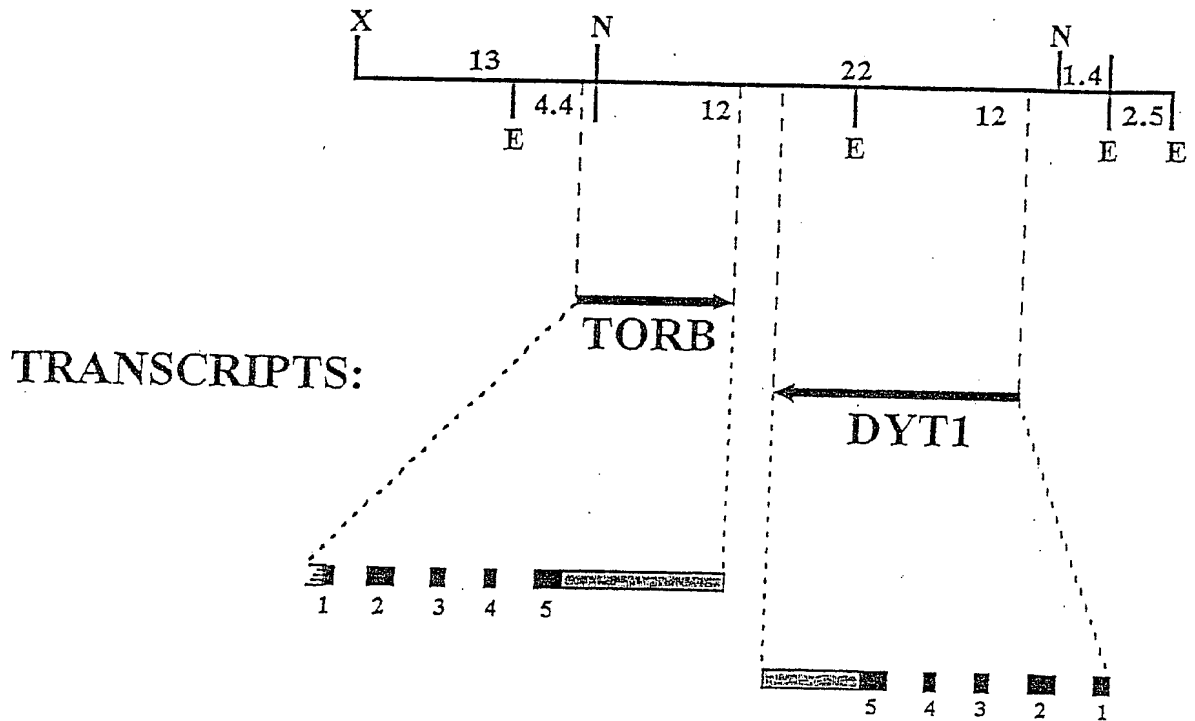


FIG. 7

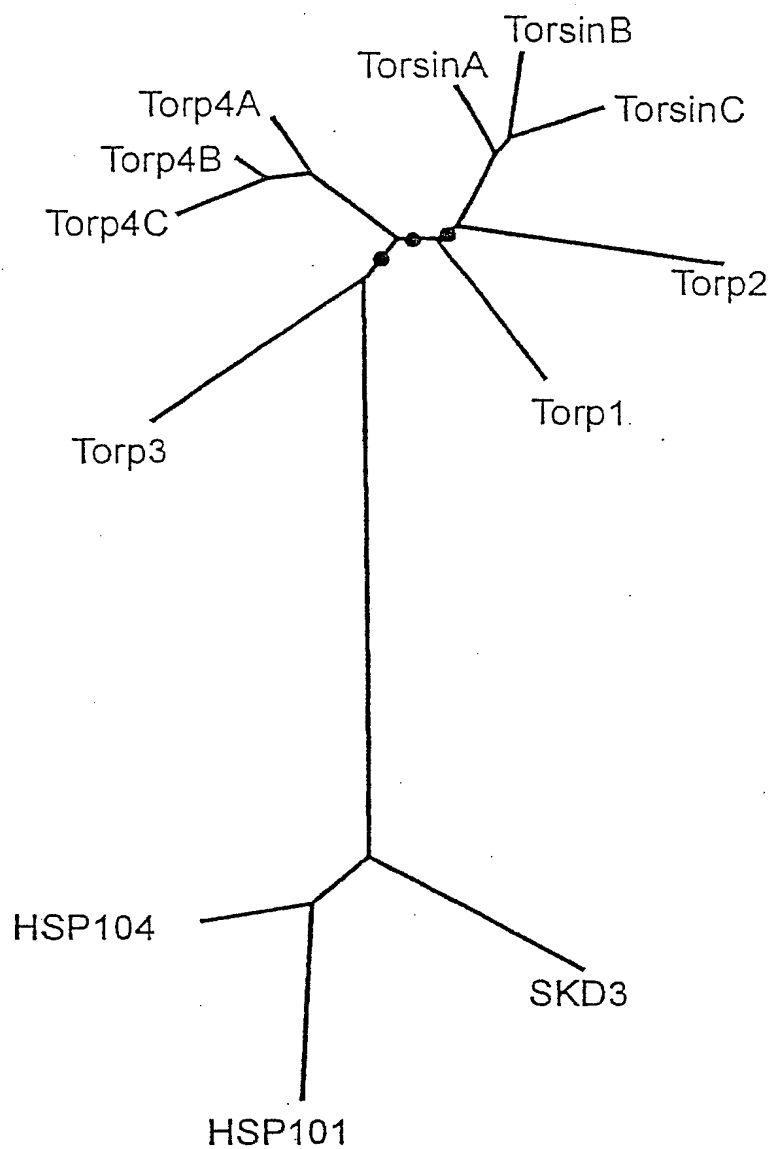


FIG. 8

FIG. 9A

*DYT1*

| Exon | Size (bp) | 3' end of exon          | 5' splice site (SEQ ID NO) | Intron (kb) <sup>a</sup> | 3' splice site (SEQ ID NO) | 5' end of exon (SEQ ID NO)      | Exon |
|------|-----------|-------------------------|----------------------------|--------------------------|----------------------------|---------------------------------|------|
| 1    | 178       | ...CGG GAG G<br>R E A   | GTAGGCTGGG... (67)         | 1.2                      | ...TCCTTCCCAG (71)         | CA CTG CAG AAG... (75)<br>L G K | 2    |
| 2    | 266       | ...TTG TAC AAG<br>L Y K | GCAAGGATGG... (68)         | 1.5                      | ...TTTAATTTCAG (72)        | GAT CAG TTA...<br>D Q L         | 3    |
| 3    | 176       | ...TTT CTC AG<br>F L S  | GTAAGGTCAG... (69)         | 0.097                    | ...TGTTTTTGCAG (73)        | C AAT GCT GGA... (76)<br>N A G  | 4    |
| 4    | 128       | ...AAG AAC AG<br>K N S  | GTGAGTAGGG... (70)         | 4                        | ...TTCTTCCCAG (74)         | T GGC TTC TGG... (77)<br>G F W  | 5    |
| 5    | 251       | ...GAT GAT TGA<br>D D * |                            |                          |                            |                                 |      |

FIG. 9B

*TORB*

| Exon | Size (bp) | 3' end of exon          | 5' splice site (SEQ ID NO) | Intron (kb) <sup>a</sup> | 3' splice site (SEQ ID NO) | 5' end of exon (SEQ ID NO)      | Exon |
|------|-----------|-------------------------|----------------------------|--------------------------|----------------------------|---------------------------------|------|
| 1    | n.d.      | ...GCT TCG G<br>A S A   |                            | n.d.                     | ...GTTCTTGCAG (81)         | CT CTC AAG CTG... (85)<br>L K L | 2    |
| 2    | 266       | ...CTG TAC CAG<br>L Y Q | GCAAGAGAAC... (78)         | 3                        | ...GTTGTGTCCAG (82)        | GAC CAG TTA...<br>D Q L         | 3    |
| 3    | 176       | ...TTT CTC AG<br>F L S  | GTCAGCGGGA... (79)         | 1.8                      | ...GCAAACTCAG (83)         | C AAT GCA GGC... (86)<br>N A G  | 4    |
| 4    | 128       | ...AAA CAC AG<br>K H S  | GTGAGTCCAC... (80)         | .31                      | ...TGTTCTTGCAG (84)        | T GGC CTG TGG... (87)<br>G L W  | 5    |
| 5    | 242       | ...TTC CAC TGA<br>F H * |                            |                          |                            |                                 |      |

\*Sizes of introns were approximated by gel resolution of PCR products

FIG. 10

109270-5012260

| Type            | Number of<br>Individuals | Age of onset<br>yrs                      | Site of onset <sup>a</sup><br>(no.) | Sites involved<br>(no.)                     |
|-----------------|--------------------------|--|-------------------------------------|---|
| Early onset:    |                          |  |                                     |   |
| AJ              | 5                        | 6, 8, 8, 10, 19                          | A(4), ANL(1)                        | A(7), N(3), T(1), L(2)                      |
| NJ              | 12                       | 3, 6(2), 8, 9, 10, 11, 13, 14(2), 16, 18 | A(9), AU(1)                         | A(20), G(9)                                 |
| Potential       |                          |  |                                     |   |
| homozygosity:   |                          |  |                                     |   |
| AJ <sup>b</sup> | 5                        | 4, 6, 7, 26, 35                          | L(4), M(1)                          | L(4), M(1), N(2), P(1),<br>T(1), U(1), H(2) |
| Late onset:     |                          |  |                                     |   |
| AJ              | 1                        | 66                                       | U                                   | U   |

<sup>a</sup> Body sites: U=upper face, F=lower face, J=jaw, T=tongue, P=pharynx, L=larynx, S=speech, swallowing, A=arm, K=trunk, G=leg, N=neck, H=hearing loss. (no.=Number of individuals in group with that site affected.)

<sup>b</sup> Three of these individuals had all known AJ ancestors, one was 7/8 AJ, and one was 1/2 AJ.

| Sample<br>number   | Genotype             |         |       |                 |
|--------------------|----------------------|---------|-------|-----------------|
|                    | D9S2160 <sup>a</sup> | D9S2161 | D9S63 | D9S2162         |
| 18843              | 3,4                  | 2,2     | 8,8   | 4,4             |
| 13709              | 4,4                  | 2,6     | 14,14 | NT <sup>b</sup> |
| 14122 <sup>c</sup> | 3,3                  | 4,4     | 0,0   | 5,5             |
| 13945              | 4,4                  | 1,5     | 18,18 | NT <sup>b</sup> |
| 14040              | 2,5                  | 1,2     | 16,16 | 2,4             |

<sup>a</sup> Markers listed from centromere to telomere: D9S2160 - <40 kb - D9S2161 - 150 kb - D9S63 - 130 kb - D9S2162 (Ozelius *et al.*, 1997a).

<sup>b</sup> Position of DYT1 gene

<sup>b</sup> Not tested.

<sup>c</sup> This individual had onset at 7 years in the arm with eventual involvement of the arm and neck and a positive family history of movement disorder (father with tremor). He was also apparently homozygous for markers D9S159-D9S2158-D9S2159, which are proximal to DS2160 (total region of 100 kb).

FIG. 11

00723405-013504

FIG. 12A

| Intron Primers Used to Amplify DYT1 Exons |                              |                   |                       |
|---|------------------------------|-------------------|-----------------------|
| Exon                                      | Primer Sequence<br>(5' → 3') | SEQ. ID NO.:      | Product Size<br>(bp)* |
| 1   | GCAAAACAGGGCTTTGTACCG        | (SEQ. ID NO.: 30) |                       |
|   | AGTAGAGACGCGGGTAGATG         | (SEQ. ID NO.: 31) |                       |
|   | GCGTCTCTACTGCCTCTTCG         | (SEQ. ID NO.: 32) |                       |
|   | ATGCCCTGGTCCTAGTTCAG         | (SEQ. ID NO.: 33) |                       |
| 2   | GGTTTCGCAAGGTGCTTGGA         | (SEQ. ID NO.: 34) | 408                   |
|   | GGGATTCCAAACTTCCATCC         | (SEQ. ID NO.: 35) |                       |
| 3 and 4                                   | TCCATGGGGTTGGTAGGAAC         | (SEQ. ID NO.: 36) | 804                   |
|   | GGTGACAGAGTAAACTATCTG        | (SEQ. ID NO.: 37) |                       |
| 5   | GACCCCCAGTAGACGTTTGT         | (SEQ. ID NO.: 38) | 640                   |
|   | GTAAAAAATCATGAGCCCTGC        | (SEQ. ID NO.: 39) |                       |

FIG. 12B

| Intron Primers Used to Amplify TORB Exons |                              |                   |                       |
|---|------------------------------|-------------------|-----------------------|
| Exon                                      | Primer Sequence<br>(5' → 3') | SEQ. ID NO.:      | Product Size<br>(bp)* |
| 1   | n.d. <sup>#</sup>            |                   | -                     |
| 2   | CCAGAGTTAGTGAGCAGGTC         | (SEQ. ID NO.: 40) | 526                   |
|   | GAAGCGTTAAGGACCTCCAC         | (SEQ. ID NO.: 41) |                       |
| 3   | ATCTATCTCTGCCAATTTCAC        | (SEQ. ID NO.: 42) | 466                   |
|   | GTCCTGGTAAACAAAGTGCTG        | (SEQ. ID NO.: 43) |                       |
| 4   | TGGGGTTACTCTATGTTGGTC        | (SEQ. ID NO.: 44) | 440                   |
|   | CTAGCACAGTATGCCCTAAG         | (SEQ. ID NO.: 45) |                       |
| 5   | TGAGGAATGTGCTGAGGGTC         | (SEQ. ID NO.: 46) | 333                   |
|   | GCTGTCTCCTACCCCATCTG         | (SEQ. ID NO.: 47) |                       |

\*PCR products were generated using oligonucleotides synthesized from intronic sequences, and accordingly the size of each product includes both intron and exon sequence.

<sup>#</sup>Not done. It was not possible to identify primers which could consistently PCR this exon.

| <i>Protein</i> | <i>Organism</i> | <i>Gene</i> | <i>Locus</i>         | <i>Accession</i> | <i>UniGene</i> |
|----------------|-----------------|-------------|----------------------|------------------|----------------|
| hTorsinA       | human           | DYT1        | Chr.9, D9S159-D9S164 | AF007871         | Hs.19261       |
| mTorsinA       | mouse           |             |                      | AA230756         | Mm.40438       |
| rTorsinA       | rat             |             |                      | AA850233         | Rn.20041       |
| sTorsinA       | pig             |             |                      | AU058534         |                |
| hTorsinB       | human           | TORB        | Chr.9, D9S159-D9S164 | AF007872         | Hs.5091        |
| mTorsinB       | mouse           |             |                      | AA596988         |                |
| drTorsinC      | zebrafish       |             |                      | AA542632         |                |
| hTorp1         | human           | TORP1       |                      | AA873275         | Hs.59038       |
| mTorp1         | mouse           |             |                      | AA981789         | Mm.33875       |
| rTorp1         | rat             |             |                      | H31561           |                |
| hTorp2         | human           | TORP2       |                      | AA150869         | Hs.26267       |
| mTorp2         | mouse           |             |                      | AA791729         |                |
| dmTorp3        | fruitfly        | EG:84H4.1   | DMC84H4              | AL031766         |                |
| ceTorp4A       | nematode        | F44G4.1     | CEC18E9              | P54073           |                |
| ceTorp4B       | nematode        | Y37A1B.12   | CEY37A1B             | AL023835         |                |
| ceTorp4C       | nematode        | Y37A1B.13   | CEY37A1B             | AL023835         |                |

FIG. 13

0973406-01590  
 105210-99F2269



INTRON 1 OF DYT1 GENE

FIG. 14A: Clone 1:

23g14-2-7050.cDNA (Length: 283) SEQ ID NO.: 48

1     gtaggctggg gcgggggctg gaggctgggg ctggggctgg ggctggggcga  
 51     tggcactagg **gctgaactag** **gaccagggca** tggagaatgg aggatggagg  
 101    ccgggggatg gcaccagggc cgggctagga ctagggctgg agcggggcct  
 151    gggggctggg gctggggcat ggcactaggg cgggttgggg ctggggctgg  
 201    ggctggggga tggagcgggg ccgggggctg ggggtggggc tgggggatcg  
 251    actagggctg gnttaggacc aggcgggttg cat

Bold = primer 4 (reverse sequence) from FIG. 12A

Underline = 5' splice sequence from Intron 1 FIG. 9A

FIG. 14B: Clone 2:

Harvey7-23g14-2.cDNA (Length: 375) SEQ ID NO.: 49

1     ggatgggtgga tggaggctgg gggatggcag tagggccggg ctaggactgg  
 51     ggctggagcg gagtttgggg ctggggctca ggagcggggg ctggggctgg  
 101    ggctggggct gggggatggc actagggcag gccggggtag gggtcacatc  
 151    ccaggagggc cgggctgggc agagctgagt ccgcgggggc cggaccccg  
 201    aagccaagcn gccggcctgc aggatgaggc ctggctcttc ggccatgacc  
 251    acagacgtgc cagacttaag tacggagacc tgaggagcca ggctgcagtt  
 301    ggcctacttt ncnctaagct gggggtggac cagtggtaac ctctccgaa  
 351    gtgggttctg ctctttctag cctag

FIG. 14C: Clone 3:

23g1-Harvey11.cDNA (Length: 439) SEQ ID NO.: 50

1     ccactgccac tgccaccagt ttgcaccctt aaccctgtgn ctgctcctcc  
 51     caccccaagg cagagccggn gaaaggaaac agtttgggtcc ctcttggtcg  
 101    gctgcggaag agtctcacca tccttctgtc tccgtagcta gaaaggaggc  
 151    agaaccacac ttcggaggga gggtaccact ggtccacccc cagcttagcg  
 201    caaagtaggc caacctgcat gcctggnnct cctcaggntc tgcctactta  
 251    agtctggcag ctctnnntca tggccgaggt agccaggctc atcctgcagg  
 301    nncengccnn ttgncttncc ggggtntcgn nccccgtac tcagctcgtc  
 351    cagccggcct ctggatgtga cctaccgctg ctagtgcac ccagccagcc  
 401    agccagccgt ctagccagcc aactgctcag ccagtctag

FIG. 14D: Clone 4:

23g1-Harvey6.cDNA (Length: 378) SEQ ID NO.: 51

1     ctgggaaaga caaagccaat caggagtggg gaagaaacac ggcaaaatgt  
 51     agccacattt acagcccata aganagccag caaagccgtc tagcctccaa  
 101    **gcaccttgcg** **aaacctcaag** tactgcggtc tggttaagctc ctggcccaga  
 151    ggggacggcg gtccaggng cctcccttt gctggtcctg cctattctaa  
 201    agccctggcc cgnctccttc ccgaaaagcc ccttggtgcc actgccactg  
 251    ccaccanttt gcncctctac ccctgtntct ctcctccac cccaaggcag  
 301    atgcggngg ngaaaggaaa cantttggtc cctcctggtc ggctcngnga  
 351    agactcctca ccatccttcc tgtcttcc

Bold = primer 5 from FIG. 12A

Italics = sequence overlap between Clone 4 and Clone 3

Underline = 3' splice site from FIG. 9A

23g14-2-7050

FIG. 14E: Clone 4:

23g1-Harvey6.cDNA (Length: 388) SEQ ID NO.: 88

```
1      ctgggaaaga ctgggaaaga caaagccaat caggagtggg gaagaaacac
51     ggcaaaatgt agccacattt acagcccata aganagccag caaagccgtc
101    tagcctccaa gcaccttgcg aaacctcaag tactgcggtc tggtaagctc
151    ctggcccaga ggggacggcg gtccagggng ccctcccttt gctggtcctg
201    cctattctaa agccctgggc cgnctccttc ccgaaaagcc ccttggtgcc
251    actgccactg ccaccanttt gcncctctac ccctgtnctg ctcctccac
301    cccaaggcag atgcggngg ngaaaggaaa cantttggtc cctcctggtc
351    ggctcgngga agactcctca ccataccttcc tgtcttcc
```

Bold = primer 5 from FIG. 12A

Italics = sequence overlap between Clone 4 and Clone 3

Underline = 3' splice site from FIG. 9A

B  
a  
r  
c  
l  
a  
b  
o  
r  
a  
t  
o  
r  
y

# INTRON 2 DYT1 GENE

FIG. 15A: Clone 1:

29a5-6343.cDNA (Length: 400) SEQ ID NO.: 52

```

1    gaatattttac gaggggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51   ccacattgct ctttccacat gcttcaaaca tcaccttgta caaggcaagg
101  atggaagttt ggaatccctt cctggatgtc atcggggttg gggctctctt
151  gttgtgggat gagatttggg agttctatgt tgaaatgagt gagcccgga
201  aacggttcat gtctcagttc cccttggaag ggtgtagaag ttaagagttt
251  gagatgcgtg gagcagttaa taccatcaaa gctttgtggg gggttctgaa
301  aatcgggtcca gtgagtatgt agggtcacatg gatttttagag gtggacatga
351  tcaaattccat cttagagatc aacacatctc actcattttt attttcttat
  
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15B: Clone 1:

29a5-6343.cDNA (Length: 402) SEQ ID NO.: 89

```

1    gaatattttac gaggggtggtc tgaacagtga ctatgtccac ctgtttgtgg
51   ccacattgct ctttccacat gcttcaaaca tcaccttgta caaggcaagg
101  atggaagttt ggaatccctt cctggatgtc atcggggttg gggctctctt
151  gttgtgggat gagatttggg agttctatgt tgaaatgagt gagcccgga
201  aacggttcat gtctcagttc cccttggaag ggtgtagaag ttaagagttt
251  gagatgcgtg gagcagttaa taccatcaaa gctttgtggg gggttctgaa
301  aatcgggtcca gtgagtatgt agggtcacatg gatttttagag gtggacatga
351  tcaaattccat cttagagatc aacacatctc actcattttt attttcttat
401  tt
  
```

Bold = primer 6 from FIG. 12A

Underline = 5' splice site sequence for intron 2 from FIG. 9A

FIG. 15C: Clone 2:

6550-54a5s.cDNA (Length: 418) SEQ ID NO.: 53

```

1    tttggagtga gacaggactg ggttcaggtc ccagctctgc cacatatagt
51   cttgggcaag tggagtaagc gctctctgtg cctcagttcc ctcactctgta
101  aaatgagaac gatagtgcc actccatggg gttggttagga acaaagaaga
151  ttttgggcat gtaaagtctt tagtgccgag tgcacagtgg tctgtaagtg
201  aagctgcggt tcttagtggt agaaggagct gattgatggc cctggctgag
251  aactttgtgt tcgctttttc ccnttttaat tcaggatcag ttacagttgt
301  ggattcgagg caacgtgagt gcctgtgcca ggtccatctt catatttgat
351  gaaatggata agatgcatgc aggcctcata gatgcctntca ancctttcct
401  cgactattat gacctggg
  
```

Bold = primer 7 from FIG. 12a

Underline = 3' splice sequence for intron 2 from FIG. 9A

Italics = EXON 3 sequence

INTRON 3 DYT1

FIG. 16A: Clone 1:

6202-54a5.cDNA (Length: 198) SEQ ID NO.: 54

```
1      ctcgactatt atgacctggt ggatgggggc tcctaccaga aagccatggt
51     catatttctc aggtaagggtc agggctagga catgatggat gggccccgag
101    cccaagcctc tgagctccag gagaaaaccc tgtccttacc cactgggatt
151    gttttgcagc aatgctggag cagaaaggat cacagatgtg tttggatt
```

FIG. 16B: Clone 1:

6202-54a5.cDNA (Length: 200) SEQ ID NO.: 90

```
1      ctcgactatt atgacctggt ggatgggggc tcctaccaga aagccatggt
51     catatttctc aggtaagggtc agggctagga catgatggat gggccccgag
101    cccaagcctc tgagctccag gagaaaaccc tgtccttacc cactgggatt
151    gttttgcagc aatgctggag cagaaaggat cacagatgtg gctttggatt
```

Bold = EXON

Underline = sequence from for 5' splice site sequence and 3' splice site sequence, respectively from FIG. 9A

0972105-0450

INTRON 4 DYT1

FIG. 17A: Clone 1:

Intron 4-5 prime.cDNA (Length: 535) SEQ ID NO.: 55

1 GTCTGTGTCG GTTTTCAATA ACAAGAACAG gTGAGTAGGG CCATCCACCG  
51 CCAGTCCCAT CTGGTTCCTA ATCCTGCACC CTAAGTGTTA AAAGCATCAG  
101 GGTCACCTGTC AGCATCACCT GGGAGCTGGG TAGAAAGAAA TGgAGATTCT  
151 CAGTCCCCTT CCGAGTCATG AGGGGAATCT TTGCTGATGA ACTCCAGGTA  
201 ACTTTTATGA AACTAATGT TTGACAAGTG CTGTTTTATT TTTATTTTTC  
251 **AGATAGTTTT** **ACTCTGTCAC** CTAGGCTGGA GTGCAGTGGC GTAACCTTGC  
301 CTCACTGCAA CCTCTGCCTC CCGGGCTCAA GCGATTCTTG TGCCTCAGCC  
351 TCCTGAGTAG CTGGGATTAC AGGTGCACAC CATGCCCAAG CNAATATTTT  
401 GTATTTTTTAG TAGAGANGGG GCCCCGTNCA TGTTAACCAG GCTGGTCTTG  
451 AACTNTTACC TCAGGTGAGT CCNCCACCTC GGCCTCCCAA AGTGCTGGGA  
501 TTACAGGCGT GAGCCACTGT GTCTCAGCTT ATTTTT

Italics = EXON sequence

Underline = 5' splice sequence from FIG. 9A

Bold = primer 8 from FIG. 12A

FIG. 17B: Clone 2:

Intron 4-3 prime.cDNA (Length: 1302) SEQ ID NO.: 56

1 GCCACTCCAA GCTACCATCT GAGATTGTTT CCTGCCCTAG AGTGGTAAAG  
51 GCGTGAGGTC CGTCTGCCCT CAGCTGTGTC CCCAGGCCCA GGGCGTGCCT  
101 GGCAACANNA GCAGGCCTCT GAGAACCAGC CTCCCACGTG AGTTCATGAT  
151 AGNAAGACAG CCCCTCGTTC CCATTCAGTG GTTGTTCTG TTCTTTYCCT  
201 GGCMATAAGC TCCACTCTGY MRTCAGCCAM ACATTTATTG AGTACCAGTT  
251 GTTGCAAAG CACTGTTGGG CATGAAAAGC ATTAACCCAG TGAATGAGGA  
301 GGAGCTTGGG TTGGGACGGA GCCMCARAAW TACATGGCAG ACCAGAAGGA  
351 AATCAGCTCA AGTAGAAARA CACGCATGGG CTCGTGGGCG ACGCAGTGTG  
401 TGCTGTGTCA TCTGGGGCTG GGAGGAAGTG TCCTGGATCA GGAGTTCCAG  
451 GAGCCCAGGA GGAGTGGACG GGTCAAGTGA GAGCCAGCCC GCAATCAGGG  
501 GAAGAAAACA CGGCCAAGGC CAGGCCTTCA CGGGGAGCCC AGCGTGGGCT  
551 GCACATCTGC ACTCTCCAGG CTAGTTTGGG TGCCCACATG CTCTGCAGGG  
601 TCTGGGCACT GTGGCAGCGG CAGCAGGCTT CCCTGTTGCT AGTCCAGCTG  
651 CTGAAACTCC AGGGAGAGTC AAAAAGTTCC CAAATACAGA GGCGTGGCTG  
701 GTAGTCCTTC CCGGGAATTC TTCTTGCTTC CCGCTTTCTG TGGAACCTCTG  
751 CTTCCCCAC TCTGCCTCTC TGCTTGTTCC TGGGCCCCAG GACCTCTTTC  
801 CCATCTTCGA TCTCTTAAGT CATACTTGG GAGGCCTCCC CCAGCCCGCC  
851 GTGTAAAGAG GGCTGTCACA GCTTCTGCTG TCACAGAAGC ATTACAATGT  
901 GCAGGTGCCT GTTAACATCT GCCTTCCCCA CTGATCTGGA GCTCCACAAG  
951 GGAGAGGGCA CACCCAGTAG GTATGTGTGG GATGGATAGG AGGGTGGATG  
1001 ACACCCAGTA GATGTGTATG GGATGGATAG GAGGGTGGAT GACACCCAGT  
1051 AGGTGTGTAT GGGATGGATG GGAGGGTGGG TGACCCCTAG TAGATGTGGG  
1101 GGGGGTGGGT GGGTGACCCC CAGTAGGTGT GTGTGGCATG GATAGGTGAC  
1151 **CCCCAGTAGA** **CGTTTGTGGG** ACGGATGGGA GGGTAGGTAA GTGACCCCCA  
1201 GGAGGCGTCT ATAGGGCAGG TGGGTGGATG TGGATGAACA GCACCTTGTT  
1251 TCTTCTTCCC AGGTGGCTTC TGGCACAGCA GCTTAATTGA CCGGAACCTC  
1301 AT

Bold = primer 9 in FIG. 12A

Underline is 3' splice site sequence from FIG. 9A

Italics is EXON 5 sequence

INTRON 1 5' from TORB

FIG 18A: Clone 1:

h59-29a5.se (Length: 240) SEQ ID NO.: 57

```
1      ggagcggccg ctcaacgctt cgggtacggc gcgcgcgcga gctgtgggtc
51     ggcgctgcgg ggggcgcggg ggcgcggggg cgcggaggga cggcctcgtg
101    ggcgcctggc acggaccggg cccgtggcat ctagacggcg gtggtcccag
151    ctgggggtggg cgggggagcgg atggggcggc ccggaaccg ttcgcnggaa
201    cgcagaagcn gtgccttgaa acactctcag atcgtgnggc
```

INTRON 1 3' from TORB

FIG. 18B: Clone 2:

5667s-29a5.Se (Length: 310) SEQ ID NO.: 58

```
1      gggaccaaag gacgtccgtc gttcccaccg accctaateg ttgcgcngtc
51     ngttcgctac ccagtagaga gacttactta cnngtnnatc gaaggaatag
101    tctgggggctt cgcaattcct ggaggtgtat tagaactttc accgtagcaa
151    actgacggag ccgggatccc acaccgcctg tgggnncgac acgggacctt
201    ttgacacgaa gaacgaaacn gtcgattctt tcacgacgca acgactacgt
251    aaaaattcca gacaaagaga gaaacaagac cccgacaaga acgtcGAGAG
301    TTCGACCTAA
```

Upper Case Letters = EXON (bottom strand)

Underline = sequence from Table 1

Bold = 2<sup>nd</sup> primer from FIG. 12B

5667s-29a5.Se

## INTRON 2 5' from TORB

FIG. 19A: Clone 1:

6101-29a5.Se (Length: 401) SEQ ID NO.: 59

```

1   CAGGAACAAC AAAAATCCCCA AGAAACCACT GACCCTTTCC TTACACGGCT
51  GGGCTGGCAC AGGCAAGAAT TTTGTCAGTN AAATTGTGGC TGAAAATCTT
101 CACCCAAAAG GTCTGAAGAG TAACTTTGTC CACCTGTTTG TATCGACTCT
151 GCACTTCCCT CATGAGCAGA AGATAAAACT GTACCAGgca agagaaccg
201 ctattatctc gtctgcaggc cagtcggact ggtccgggtg acctgctcac
251 taactctggc ctctgcttct ctttcctttg tggtgctgta gcccccggt
301 ccactgagtt aaggcacact tagtccagggt agttacaaag ctctcctaca
351 acatttctta cttggttcca aaacagtcca gtggggtagg ggatgttatt
401 t

```

Upper Case Letters = EXON

Underline = 5'splice site sequence from FIG. 9B

Bold = 1<sup>st</sup> primer from FIG. 12B

## INTRON 2 3' TORB

FIG. 19B: Clone 2:

29A5-39-11.se (Length: 238) SEQ ID NO.: 60

```

1   ttctgtaact ggtcCTGGAC CAACCATGAA AGAAGAAACA GGATGCGAAG
51  CTCAAAGGGC TGCACCAAGA GGC GCGCAGG CTCCATCTGC TCCTCATGCA
101 CTGAAGGACG AGGTCAGAGC TCTTAGAATG GCACCCTCAC CCCCCTCGC
151 TAGGTAGCAG CTTTTCTAAA ACCTTATCTC TAAAAAGTGG AAATTGGCAG
201 AGATAGATGC TAAAATGCAG AGAAGTTTTT CCTAACTC

```

Lower Case Letters = EXON

Underline = sequence from Table 1

Bold = primer 3 from FIG. 12B

INTRON 3 5' TORB

FIG. 20A: Clone 1:

39-14-29a5.Se (Length: 391) SEQ ID NO.: 61

1 GGGATCATTG ACGCAATCAA GCCGTTTCTA GACTACTACG AGCAGGTTGA  
51 CGGAGTGTCT TACCGCAAAG CCATCTTCAT CTTTCTCAGg tcagcgggag  
101 gcggtttttt ggggcacaca agcccttcat tctctcaatg ataaaatgag  
151 gtcctgagga ccatc**cagcac** **tttgtttacc** **aggacgaaag** tgcctgcttg  
201 gcacaaggca cttacctact gctttacttt tcctttgccca gtcctcagca  
251 tggcacacag tgtgggttgt ggaaatgaac taaagaaata atcactggga  
301 caggcgcggt ggctcacacc tgtcaatccn agcactttgg gnaggcatgg  
351 cgggcgggatc acaggagatc gagacatctg ctaacatgnt g

Upper Case Letters = EXON

Underline = 5' splice site sequence from FIG. 9B

Bold = primer 4 from FIG. 12B

INTRON 3 3' TORB

FIG. 20B: Clone 2:

5665s-54a5.Se (Length: 373) SEQ ID NO.: 62

1 gtaagacaca gagtcttttt tnttttttag accgagtntc attnttggtg  
51 ccnangctgg agtgcaatgg catgatctcg gctcgctgca acctccacct  
101 cccggrttca aacgattctc ccacctcagc ctcccatgta gctgggatta  
151 cagncatgca ccaccattag cctggctaata ttttggtgtt ttagtagaga  
201 **tggtgttact** **ctatgttggt** caggctggcc ttgaactccc gacctcaggt  
251 gatctacctg cctcggcctc ccaaagtgt gggattacag ccatgagcna  
301 ccacnscnan cagacncaga agtcttaata tgtgatttta atctttattt  
351 ctctggcaaaa ctcagCAATG CAG

Upper Case Letters = EXON

Underline = 3' splice site sequence from FIG. 9B

Bold = primer 5 from FIG. 12B



INTRON 4 TORB

FIG. 21: Clone 1:

intron4torb.se (Length: 310) SEQ ID NO.: 63

```
1      gtgagtcac cagggtaaag gagcccctta actgtccagc agtgagccgt
51     ctgctctttc attgagtgtt tgcacaaagc cacaggatcc cactggattt
101    cctcactttg ctaaagtcag gaattttctt agggcatact gtgctagaaa
151    ccagtgagtg agtgtccagc tgagtcctcg atgggcttgt tgcacactga
201    caagagacnc tctcaagggg tacggacatg aggaatgtgc tgagggtcgg
251    gactggagct tggccaggtg gcggtggtgg caggaaaccc agctgtgtct
301    tggtctgcag
```

Underline = 5' splice site sequence from FIG. 9B

Bold = primer 6 from FIG. 12B

Underline italics = 3' splice site sequence from FIG. 9B

Bold italics = primer 7 from FIG. 12B

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